



Lens-based glaucoma surgery: Using cataract surgery to reduce intraocular pressure

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Cataract surgery has been demonstrated to lower intraocular pressure (IOP) in eyes with glaucoma. The evidence is strong in angle-closure patients that cataract surgery improves IOP and dramatically reduces the future risk for IOP spikes and acute attacks. Randomized controlled trials (RCTs) have shown that cataract surgery may be preferable to laser iridotomy or phacotrabeculectomy. The data are so convincing that an RCT has been undertaken to assess whether clear lens extraction may be appropriate following acute attacks and in cases of uncontrolled IOP. The case favoring cataract surgery in open-angle glaucoma (OAG) is more controversial. Impressive IOP reduction has been shown in OAG patients when the patients are stratified by preoperative IOP. The patients with the highest preoperative IOPs have pressure reductions up to 8.5 mm Hg. However, these findings have been criticized for methodological weaknesses. Combining cataract surgery with microinvasive glaucoma surgery in phaco-plus procedures provides further options for lens-based glaucoma surgery.

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A growing body of evidence supports the view that cataract surgery in glaucoma patients significantly reduces intraocular pressure (IOP).^{1–12} This has led to the concept of lens-based glaucoma surgery.¹³ Cataract surgery lowers IOP in patients with narrow or closed angles as well as in those with open angles. In angle closure, cataract surgery has gained widespread acceptance as a valuable glaucoma intervention.^{8–12,14} However, there is more controversy about the role of cataract removal in open-angle glaucoma (OAG). Some investigators question the data quality of the studies showing pressure lowering in OAG.^{14–17} Some strongly oppose the conclusion

that cataract surgery should be recommended as a glaucoma therapy for OAG.^{14,18}

The outcome of the debate over the role of cataract surgery in patients with glaucoma has major public health implications. Some glaucoma surgeons have proposed that the diagnosis of glaucoma should be considered a reason to perform cataract surgery earlier.¹³ More than 20 million Americans older than 40 years have symptoms from cataracts,^A and more than 3 million cataract surgeries are performed in the United States each year.^B A recent review of a large Medicare database found that 19.1% of patients with a diagnosis of cataract had a coexisting diagnosis of glaucoma.¹⁹ If the presence of glaucoma leads to earlier lens removal, the volume of cataract surgery could increase dramatically.

CATARACT SURGERY AS A TREATMENT FOR OPEN-ANGLE GLAUCOMA

Surgeons have been aware that cataract surgery decreased IOP in patients with open angles, but the studies generally found that the reduction was relatively small.^{4,20–23} A 2002 metaanalysis found that phacoemulsification usually reduced IOP by 2 to 4 mm Hg.¹⁷ However, the authors graded the evidence

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as “weak (but consistent)” and commented that there were no randomized clinical trials (RCTs) and no untreated control groups among the studies. The modest pressure reduction demonstrated in these studies did not lead surgeons to alter decisions regarding cataract surgery in glaucoma patients.

In a breakthrough insight, Poley et al.³ found that postoperative pressure reduction was proportional to the preoperative IOP. Most previous studies had reported only the mean IOP reduction, which was usually 1 to 3 mm Hg. Studies that failed to stratify patients by preoperative IOP may have missed the larger pressure reductions in patients with higher preoperative pressures. Even the studies that did find an association between higher preoperative pressures and larger postoperative pressure reductions did not stratify the data by preoperative pressures.^{10,20,24}

By stratifying the data, Poley et al.^{3,5} demonstrated that patients with more elevated IOPs had pressure reductions that were much larger than the mean pressure reduction for the entire group. This was a critical observation since patients with higher pressures need pressure lowering the most. These authors showed that glaucoma patients with higher pressures experienced pressure reductions of up to 8.5 mm Hg following cataract surgery.⁵ This level of IOP improvement is very significant. Dr. Richard Lindstrom devoted his 2008 American Academy of Ophthalmology Kelman lecture to discussing the evidence for recommending cataract surgery as a treatment for glaucoma.^C

The first Poley et al. study³ was a retrospective review of 588 eyes that did not have glaucoma. They were grouped according to the preoperative IOP. The group with the highest preoperative pressures (31 to 23 mm Hg) experienced a reduction of 6.5 mm Hg. The next highest group (22 to 20 mm Hg) experienced a reduction of 4.8 mm Hg. The magnitude of IOP reduction diminished gradually and proportionally with lower preoperative pressures.

In a separate study, Poley et al.⁵ reviewed 124 eyes with glaucoma and also found that cataract surgery reduced IOP in proportion to the preoperative IOP. The group with the highest IOP (29 to 23 mm Hg) experienced an IOP reduction of 8.5 mm Hg. In the next highest IOP group (22 to 20 mm Hg), the IOP decreased by 4.6 mm Hg. These pressure reductions would be comparable to the addition of 1 or even 2 glaucoma medications.

Two recent RCTs have shown substantial pressure reduction from phacoemulsification surgery.^{1,2} The control group in the pivotal study of the iStent (Glaukos Corp.) received cataract surgery alone, without the implantation of an iStent. This control group had a mean and standard deviation IOP reduction of 8.5 mm Hg

± 4.3 (SD).² The Ocular Hypertensive Treatment Study (OHTS)² found a mean IOP reduction of 4.0 mm Hg in the 63 untreated patients who had cataract surgery during the 14-year study.² This is a 16.5% reduction from the baseline IOP. As in the Poley et al. studies,^{3,5} the pressure reduction was proportional to the preoperative IOP. The patient group with the highest preoperative IOP had a pressure reduction of 22.5%.

The mechanisms of pressure lowering following phacoemulsification are not known. Poley et al.⁵ hypothesize that age-related thickening of the crystalline lens narrows the anterior chamber angle and contributes to the onset of pressure elevation and eventually glaucoma. They propose that pressure elevation associated with lens expansion should be considered as a type of phacomorphic ocular hypertension. They further speculate that removing the lens lowers the IOP by widening the angle and improving the intrinsic pumping mechanism in the canal that was proposed by Johnstone.²⁵ Issa et al.²⁴ found that pressure lowering after phacoemulsification was highly correlated with preoperative IOP and the anterior chamber depth (ACD). However, they did not find a statistically significant relationship between IOP reduction and lens thickness, although lens thickness was inversely related to ACD.

CONTROVERSIES REGARDING CATARACT SURGERY AS A TREATMENT FOR OPEN-ANGLE GLAUCOMA

Studies demonstrating IOP reduction following cataract surgery have been criticized. Most of the studies are retrospective, and many use only a single pressure measurement for the preoperative value. A single pressure may not be representative and makes these studies susceptible to problems of regression to the mean.^{13,15,16} Another criticism is that many studies do not include gonioscopy. This raises the possibility of unintentionally including cases of angle closure. The study by Samuelson et al.¹ did not have an untreated control group, and there was no definite protocol for the use of medications following cataract surgery. The OHTS had a small sample size (63 patients) and no patients who had glaucoma damage or who were receiving glaucoma treatment.²

The weaknesses of the studies cited above have led numerous investigators to conclude that the data quality is inadequate to justify a recommendation for cataract surgery as a glaucoma treatment.^{14–18} One investigator group felt strongly enough to make this the title of its review.¹⁸ The authors did not dispute the modest IOP reduction found in most studies, but they objected to stories in trade journals that they said exaggerated the potential IOP-lowering effect of cataract surgery.

A separate line of reasoning—unrelated to the lowering of IOP—may favor performing cataract surgery earlier in eyes that may eventually require glaucoma surgery. The presence of even early cataract often creates a challenge in the surgical management of glaucoma. Cataract progression frequently follows any glaucoma surgery, such as a tube-shunt or a trabeculectomy. This is especially true in older patients in whom decreased vision is a common outcome after successful glaucoma surgery. Few things are more disappointing than achieving a target IOP with glaucoma surgery only to have the patient experience decreased vision from cataract. The high risk for cataract problems has led Jampel²⁶ to observe that patients having trabeculectomy may be more likely to require cataract surgery than to achieve an optimal IOP.

Cataract surgery performed following trabeculectomy is technically more difficult and carries more risk. For example, hypotony may make IOL power determination less accurate and astigmatism correction more uncertain. Cataract surgery following filtration surgery may also threaten the functioning of the bleb. On the other hand, cataract surgery performed prior to glaucoma surgery takes advantage of whatever IOP reduction may occur and avoids the ongoing infection risk of a filtering bleb. Furthermore, removing the crystalline lens may simplify postoperative management, especially reforming shallow or flat anterior chambers. Many surgeons would prefer to perform glaucoma surgery in a pseudophakic eye than a phakic eye. Given the high likelihood of cataract formation or progression after glaucoma surgery, removing even mild cataracts may be in the best interest of patients with a high risk for eventually needing glaucoma surgery.^{13,26}

CATARACT SURGERY AS A TREATMENT FOR ANGLE-CLOSURE GLAUCOMA

Primary angle-closure glaucoma (PACG) may affect 15 million people worldwide.²⁷ The acute form is characterized by sudden pressure elevations requiring emergency laser treatment or incisional surgery. Episodic pressure spikes or a progressive increase in IOP may continue even after laser iridotomy. Chronic angle closure has less dramatic IOP elevations but may also be associated with occasional pressure spikes. Primary-angle glaucoma causes almost one-half of the blindness attributed to glaucoma worldwide. It can be fundamentally improved, if not fully “cured,” when treated at the appropriate time with laser iridotomy or cataract surgery.^{8–12,28–31} Therefore, much of the PACG blindness may be preventable.

The anatomy of angle-closure eyes supports a therapeutic role for lens removal.^{31–36} Angle closure occurs

in short eyes with shallow anterior chambers. The increasing thickness of the aging lens may also contribute to a progressive narrowing of the angle. Laser iridotomy widens the anterior chamber angle, but some iridotrabecular contact persists in most patients and angle closure may progress despite a patient iridectomy.³² Performing cataract surgery may anatomically improve the PACG eye more profoundly than an iridotomy because removing the lens mass causes a greater deepening of the chamber and opening of the angle. This may reduce or even eliminate the risk for blindness from an acute attack as well as a chronic increase in IOP.

Cataract surgery has been found to be a more effective treatment for an attack of acute primary angle closure than laser iridotomy.^{8,9} Lam et al.⁸ randomized patients with acute primary angle closure to early phacoemulsification or laser iridotomy after the attack was successfully treated with medications. Compared with the iridotomy eyes, the phacoemulsification eyes had dramatically fewer IOP elevations and lower mean IOPs, required fewer medications, and had deeper angles following lens removal. The authors conclude that in acute primary angle-closure eyes presenting with pressures greater than 55 mm Hg, phacoemulsification was a “definitive treatment” for preventing subsequent IOP elevations.

Cataract surgery alone has been compared with combined phacotrabeculectomy in treating chronic angle-closure glaucoma eyes with IOPs that were both controlled and uncontrolled.^{28,29} Phacoemulsification alone reduced IOP in both groups as well as the number of medications required for medical control. In the medically uncontrolled study, the IOP was reduced nearly 8 mm Hg with phacoemulsification alone and the effect lasted for the 2 years of the study.²⁹ The patients were not stratified by preoperative IOP. Control of the glaucoma as defined in the study was achieved in more than 90% of patients in both treatment groups. The phacotrabeculectomy group required a mean of 1.25 fewer postoperative medications to achieve IOP control than the group having cataract surgery alone.

The phacotrabeculectomy group had a higher complication rate than the cataract surgery alone group.^{29,37} Two patients lost central acuity despite good IOP control (“snuff out”) and 2 others lost vision from progressive optic atrophy.²⁹ The authors conclude that phacoemulsification alone is a “viable surgical alternative” to combined phacotrabeculectomy whether the IOP prior to surgery is controlled. Although adding the trabeculectomy achieved a slightly lower IOP, the authors preferred phacoemulsification alone because of the decreased complication rate. These studies found that 14.8% of uncontrolled

patients and 2.9% of controlled patients eventually required a trabeculectomy.^{28,29} However, the authors said there was no available evidence showing that the eyes needing subsequent trabeculectomy would have worse outcomes than eyes having primary combined surgery.

ROLE OF CLEAR LENS EXTRACTION IN ANGLE-CLOSURE GLAUCOMA

The argument favoring cataract surgery as a treatment for angle closure is bolstered by the observations that removal of the lens deepens the chamber and opens the angle.^{33–35} Combining this anatomical evidence with the clinical success of cataract surgery has led to discussions about whether clear lens extraction (CLE) should be recommended for patients with angle closure.^{38,39} To our knowledge, there are no published studies of the role of CLE in treating angle closure. However, if the anterior segment anatomy is the problem, removing a clear lens may have the same positive effects as removing a cloudy lens. The possible role of CLE in PACG has been thoughtfully reviewed by Thomas et al.³⁸ and Walland and Thomas.³⁹ Thomas et al.³⁸ question whether clear lens surgery is already being used in clinical practice because of the large number of articles discussing it in non-peer-reviewed trade journals. Because of the absence of peer-reviewed literature, Thomas et al.³⁸ extrapolate from data acquired in studies in which cataracts were removed to treat PACG. They reach an assessment about RLE based on the risks of intervention versus the likelihood of preventing a serious PACG issue.

In acute primary angle closure, Thomas et al.³⁸ acknowledge that Lam et al.⁸ have presented compelling data in a RCT that cataract surgery is preferable to laser peripheral iridotomy (LPI). However, these authors warn about the risks of cataract surgery in eyes recovering from an acute attack. They suggest the more conservative approach of LPI and medical therapy with lens extraction reserved for patients who continue to have uncontrolled pressures.

In fellow eyes of patients who have suffered an attack of acute primary angle closure, Thomas et al.³⁸ recommend LPI rather than CLE. In their assessment, the low risk for acute primary angle closure following LPI does not justify a CLE. However, they do recommend consideration of CLE when IOP is elevated despite medical therapy and a significant portion of the angle has not been permanently closed by peripheral anterior synechiae.

The success of cataract surgery alone in primary angle closure may depend on the reversibility of angle damage and the target IOP. Patients with primary angle closure by definition have narrow angles and

some appositional closure in at least 3 quadrants with IOP elevation but no glaucoma damage. The authors do not recommend CLE unless LPI and medical therapy are not effective.^{38,39} Goniosynechialysis can be combined with CLE, and this may help reduce the IOP.⁴⁰ However, there are no studies comparing the risks and benefits of phaco plus goniosynechialysis with phacoemulsification alone.

Other critical issues for CLE are how to define the extent of angle closure and how to predict the degree of reversibility. Although most clinicians rely on gonioscopy to assess angle closure, this evaluation takes great skill to perform and is highly subjective. Ultrasound and optical coherence tomography can also image the angle, but the techniques and standards for these modalities are evolving.⁴¹ A second problem is that the angle appearance may not correlate with the severity of the glaucoma. Previous iridotrabecular contact may impair outflow even though the angle appears open.³² The IOP level and the response to LPI or cataract surgery may not correlate with the appearance of the angle. Although a greater extent of angle closure on gonioscopy may in general be associated with a larger IOP elevation, many patients with similar amounts of angle closure may have different pressures. Therefore, predicting which angle-closure patients will benefit from lens removal—whether clear or cataractous—remains uncertain.

Concern about recommendations for CLE encouraging high volumes of unnecessary surgery may be unfounded for 2 reasons. First, truly clear lenses are not common following an acute attack or in patients with serious and chronic angle-closure issues. Second, these patients have multiple surgical risk factors. The complexity of these cases may be more likely to prompt referral to a specialist than to increase inappropriate surgery on clear lenses.

Our practice has performed CLEs for angle-closure issues in more than 20 patients over the past several years. These patients have been highly hyperopic (up to +18.0 diopters) with short eyes (2 eyes were 15.0 mm in axial length) and very shallow chambers, some requiring pars plana vitrectomy to have enough anterior chamber room for surgery. They often have small fixed pupils from previous pilocarpine use and/or iris epithelium adherence to the anterior lens surface from repeated laser iridoplasty in an unsuccessful attempt to pull the iris out of the angle. These risk factors make cataract surgery or CLE in this group very difficult. Additionally, after the challenges of the operation, there is a high risk for postoperative malignant glaucoma and other serious complications.

Although the challenges of advanced angle closure may not invite large numbers of CLEs, removing a clear lens may be a reasonable option in less severe

cases. For example, we recently treated a 45-year-old woman with PACG and a clear lens who had an LPI and iridoplasty but had an IOP higher than 30 mm Hg on maximal medications. She was starting to show increased optic nerve cupping in that eye although her visual field remained full. Cataract surgery alone would have been easy to recommend if her eye had had some cataract. However, in the absence of cataract, many surgeons would have recommended a trabeculectomy.

Once we knew that pressure-lowering surgery was necessary in this patient, we recommended a CLE. However, we knew this was controversial and so we obtained a second opinion from another glaucoma specialist. He recommended a trabeculectomy. After much discussion and careful deliberation, the patient elected to have CLE. Five years later, she has a normal IOP on no medications. This is fortunate as she is much better off without a tube or a trabeculectomy. This single case is representative of many other cases in our practice in which pressures have normalized with cataract surgery alone. However, a small number of cases have required a subsequent trabeculectomy. Tham et al.³⁰ put this risk at 14.8% for patients such as ours with uncontrolled IOP. However, the lenses in their patients were cataractous rather than clear.

It is useful to examine the likely scenario if the advice of the consultant had been followed and the patient had been treated with a trabeculectomy. This 45-year-old woman would have had a high risk for developing a cataract. Jampel²⁶ wrote that following a trabeculectomy, the risk for requiring cataract

surgery was approximately 50%. Furthermore, subsequent cataract surgery has more risk, threatens the function of the bleb, and any benefit to the IOP of removing the lens primarily has been lost. These problems are all in addition to the ongoing risk for bleb infection. It seems prudent to extrapolate the findings of Tham et al.³⁰ to this case and avoid this daunting group of risks by performing CLE in uncontrolled PACG. A trabeculectomy can be done later if necessary.

MICROINVASIVE GLAUCOMA SURGERY COMBINED WITH CATARACT SURGERY

The emergence of microinvasive glaucoma surgeries may continue to change our approach to cataract surgery in glaucoma patients. Microinvasive glaucoma surgeries include implantation of the iStent (Glaukos Corp.), trabeculotomy with the Trabectome (NeoMedix, Inc.), and endocyclophotocoagulation.^{2,42,43} These procedures can be combined easily with cataract surgery without a significant increase in risk. The rise of microinvasive glaucoma surgeries gives cataract surgeons the option of adding a glaucoma procedure to their cataract procedures that does not have the risks of combined surgery with a trabeculectomy or tube shunt. The goal of these phaco-plus procedures is to achieve lower IOPs in glaucoma patients than performing cataract surgery alone.

In 1986, Shields⁴⁴ provided a flow diagram for selecting the appropriate operation in a patient with glaucoma who has significant cataract (Figure 1). The options in 1986 were cataract surgery alone, a

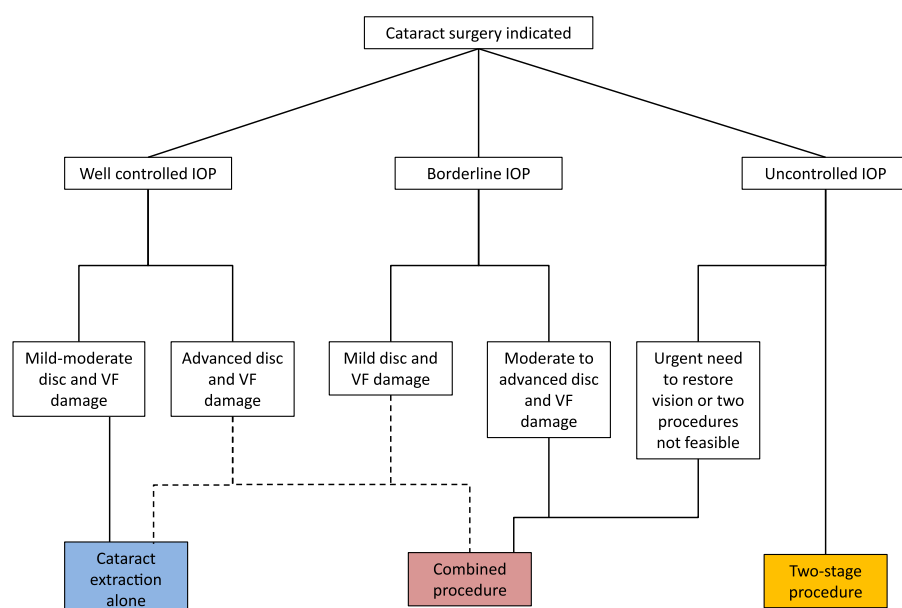


Figure 1. Surgical options for a patient with cataract and glaucoma in 1986, as originally suggested by Shields.⁴⁴ “Uncontrolled IOP” means an IOP that is greater than either cataract surgery alone or phaco-plus surgery would be expected to achieve. Dotted lines indicate options that must be weighed individually for each patient.

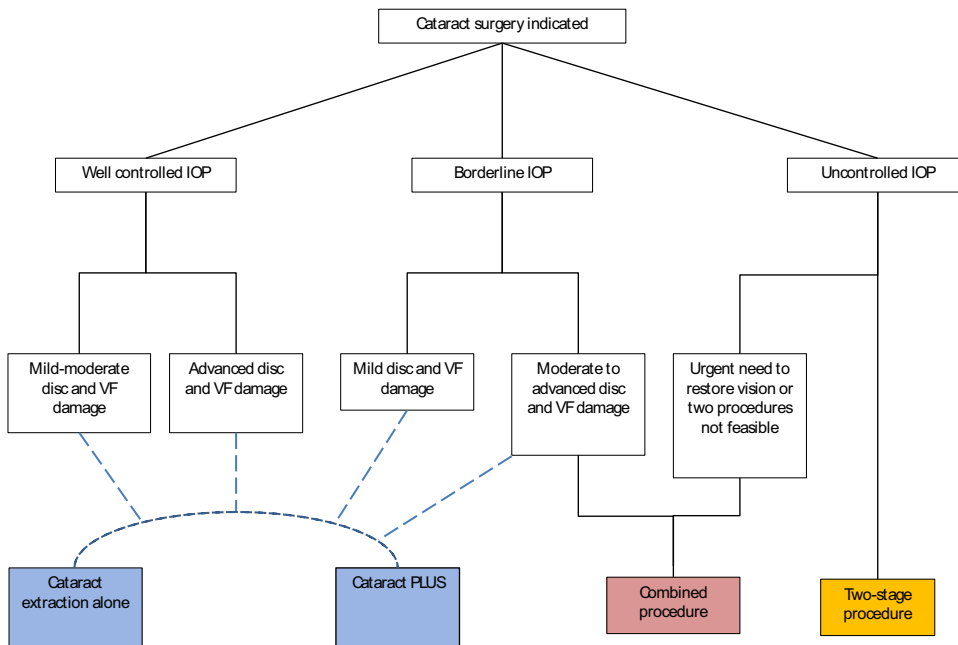


Figure 2. Surgical options for a patient with cataract and glaucoma in 2013. “Uncontrolled IOP” means an IOP that is greater than either cataract surgery alone or phaco-plus surgery would be expected to achieve. Dotted lines indicate options that must be weighed individually for each patient.

combined cataract–trabeculectomy procedure, or a staged trabeculectomy followed later by cataract surgery. This diagram has been revised to reflect current treatment strategies, which include an increasing reliance on phacoemulsification alone and also the additional option of the new phaco-plus procedures (Figure 2).

The 1986 diagram embodies the teaching at the time that combined surgery should be strongly considered if the glaucoma damage was more serious, as demonstrated by moderate to advanced damage to the disc or visual field. Current practice has shifted away from combined surgery and toward performing cataract surgery alone if the IOP is not overly elevated even in patients with greater damage. This adjustment reflects the greater awareness that cataract surgery alone may reduce IOP enough to reach the goal—even in patients with advanced disease—and also an increasing emphasis on safety. Furthermore, cataract surgery does not limit the ability to perform glaucoma surgery later. In fact, removing the lens may improve the final outcome after a trabeculectomy since the concern about subsequent cataract development is eliminated.

The option to perform phaco-plus surgery raises the question of whether these procedures may be preferable to cataract alone in glaucoma patients. Since microinvasive glaucoma surgery has an outstanding safety profile and is compatible with rapid visual recovery, the potential for additional IOP reduction makes phaco-plus an appealing alternative. The role of phaco-plus will depend on how much the

microinvasive glaucoma surgery procedure adds to the IOP lowering provided by cataract surgery alone. Few studies have attempted to answer this question. Many studies have shown impressive IOP reductions following phaco-plus procedures, but rarely has phaco alone been compared in a randomized controlled study with a phaco-plus procedure.

In summary, the provocative papers of Poley et al.^{3,5} have stimulated a healthy debate about the role of cataract surgery in OAG.^{13–16,18} The central questions are whether cataract surgery truly reduces IOP more for patients with higher IOPs and whether this reduction is clinically important. If the answers are yes, cataract surgery may deserve to be considered as a glaucoma intervention. However, further studies—RCTs with appropriate control groups—will be necessary to convince skeptical surgeons as well as governmental and third-party healthcare payers.

Modern phacoemulsification with IOL implantation has greatly benefited glaucoma patients, even without any reduction in pressure. Glaucoma patients have gained substantially from the many advances in cataract surgery, such as the move from extracapsular surgery to small-incision phacoemulsification and solving the problems of small pupils without excessive iris surgery. Furthermore, they have been helped by avoiding “casual” combined surgery where an imprecise surgical “bite” was taken out of the posterior lip of the cataract incision with the main goal of preventing a postoperative pressure spike or “because I’m there.” We see patients every day in our practices from the pre-phaco era with peripheral anterior synechiae,

secondary angle closure, chronic inflammation, and other ongoing problems from extracapsular surgery that contribute to their glaucoma. Modern phacoemulsification has helped glaucoma patients avoid the worsening of their pressure control caused by these now-avoidable complications.

The question has been asked, "Does a diagnosis of glaucoma change the indications for cataract surgery?" The answer is clearly yes. The yes is very strong for angle closure. There seem to be few clinical situations in PACG in which removal of the lens is not beneficial and preferred over laser treatment or a phacotrabeculectomy.^{8,9,28-30} The role for cataract surgery in angle closure is expanding, with even CLE being evaluated in a large RCT.³⁸ The yes may not yet be as strong for OAG but cataract surgery is now being considered in the OAG treatment paradigm at an earlier point than in the past.¹³ The role for phacoplus procedures will probably expand, but this will depend on how much each microinvasive glaucoma surgery procedure or device adds to the IOP reduction of cataract surgery alone.

The rise of cataract surgery as a focal point in glaucoma care demonstrates that we are looking at the glaucoma patient in new ways. Most glaucoma patients will eventually need cataract surgery and this must be factored into their overall treatment plan. The pressure reduction achieved by modern phacoemulsification—as well as its safety and success—has elevated lens-based glaucoma surgery to the forefront of glaucoma treatment. Whereas cataract surgery in the glaucoma patient may have been a procedure to avoid, it is becoming a procedure to embrace. Lens-based glaucoma surgery is an opportunity to help glaucoma patients see more clearly while reducing their future risk from pressure damage.

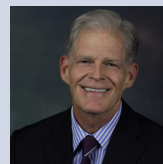
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